



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY  
AND POLLUTION PREVENTION

MEMORANDUM

DATE: 8/12/2013

SUBJECT: Human Health Risk Assessment of Vermont Chlorpyrifos Misuse

PC Code: 059101

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Petition No.: Not Applicable

Assessment Type: Single Chemical

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CAS No.: 2921-88-2

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EPA/OPP was contacted by the Vermont Department of Health (VDOH) for assistance with an enforcement case related to potential chlorpyrifos misuse. The state of Vermont developed a human health risk assessment using EPA's *SOPs for Residential Exposure Assessment*<sup>1</sup> and wipe sampling data collected from homes treated with chlorpyrifos indoors. EPA/OPP evaluated Vermont's assessment and has conducted its own human health risk assessment based on the same sampling data and information from its recent risk assessment for chlorpyrifos<sup>2</sup>. This memorandum presents the findings of this analysis.<sup>3</sup>

<sup>1</sup> <http://www.epa.gov/pesticides/science/residential-exposure-sop.html>

<sup>2</sup> [www.regulations.gov](http://www.regulations.gov) (docket ID EPA-HQ-OPP-2008-0850-0025)

<sup>3</sup> Note: The state of Vermont reviewed this document in draft form and provided comments (8/7/2013). EPA/OPP has reviewed the state's comments and incorporated changes as deemed appropriate.

## **Background**

- VDOH contacted EPA's Office of Pesticide Programs (OPP) and others to request support related to their need to assess residential exposures to chlorpyrifos following apparent misuse in many residences and institutions (~220) being investigated by the Vermont Agency of Agriculture, Food and Markets (VAAFM). There have been several conference calls and emails since that time involving various staff and representatives from EPA offices and other agencies (ATSDR, VDOH, etc.).
- Chlorpyrifos has a long history of use in the residential market. In fact, it was at one point one of the most used pesticides in the indoor residential market. The use pattern involved in this case (indoor broadcast and/or crack and crevice sprays) was previously a registered use of chlorpyrifos (prior to its cancellation in 2001).<sup>4</sup> Chlorpyrifos was phased out over a several year period based on EPA/OPP's risk assessment findings. It also had major use in residences as a pre-construction and post-construction termiticide.
- EPA/OPP has a long history of evaluating the risks associated with the residential use of pesticides. The methods currently used are described in a public document (*SOPs for Residential Exposure Assessment*).<sup>5</sup> This document and previous versions have undergone an extensive public peer review process as have many of the exposure factors used as its basis.<sup>6</sup>
- VAAFM sampled residues and collected applicator records for impacted structures, most of which are residential settings (some institutions were sampled as well). Samples of surface residues in those treated structures were collected using cotton-ball wipes soaked with methanol. This method is believed to be able to efficiently collect most deposited residues.<sup>7</sup> Samples were collected from various surfaces in these locations and at different times after application (days to months).
- VDOH defined action levels (i.e., residue levels) used to define the course of action to take for various sampling results. These values are described below.

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<sup>4</sup> <http://www.epa.gov/pesticides/reregistration/chlorpyrifos/> contains a regulatory history and links to critical documents including previous risk assessment for then existing indoor residential uses

<sup>5</sup> <http://www.epa.gov/pesticides/science/residential-exposure-sop.html>

<sup>6</sup> <http://www.epa.gov/scipoly/sap/meetings/2009/100609meeting.html>, [http://www.epa.gov/scipoly/sap/meetings/1999/092199\\_mtg.htm](http://www.epa.gov/scipoly/sap/meetings/1999/092199_mtg.htm), and [http://www.epa.gov/scipoly/sap/meetings/1997/090997\\_mtg.htm](http://www.epa.gov/scipoly/sap/meetings/1997/090997_mtg.htm)

<sup>7</sup> EPA/600/R-96-089 Camann et al (1996) which measured chlorpyrifos removal from hands with alcohol and EPA (1998) Laboratory and Field Methods to Establish a Dermal Transfer Coefficient For Residential Exposure Monitoring which quantified the efficiency of an alcohol wipe technique using malathion.

## VDOH Analysis/Data<sup>8</sup>

- The VDOH sampling data are summarized below.
  - There are ~220 unique site codes based on “unique identifier” codes.
  - A “date of sampling” is reported for only 55 of 220 locations (a location can include all samples collected for that “unique identifier”).
  - Sample collection surfaces were extremely varied and included mirrors, windows, furniture tops, boxes, walls, and baseboards. Of the ~175 samples collected (based on descriptions provided) only ~5 indicate they were on flooring.
  - Results have been reported for 18 of 55 sampled locations (N = 74)
    - 7 of 18 locations have residues >”ND”
    - 23 of 74 results have residues >”ND”
    - The mean value for all samples >ND is 0.350 ug/cm<sup>2</sup> and the highest observed value is 3.993 ug/cm<sup>2</sup>.
    - Samples were collected at different numbers of days after application ranging from 8 days to months.
- As mentioned above, VDOH has also developed “action levels” based on EPA/OPP’s *SOPs for Residential Exposure Assessment* with some notable modifications and using toxicological input values which are inconsistent with EPA/OPP’s approach.<sup>9</sup> These action levels are meant to be compared with the wipe sampling data described above to indicate a health concern which may require a mitigation action. VDOH has indicated at least 7 families have been moved from their residence based on the results of their sampling and calculated action levels. EPA/OPP offered assistance to VDOH in the development of these values. The VDOH action levels are as follows in Table 1:

Table 1. Vermont Action Levels and Associated Endpoints			
Exposure Duration	Action Range	Toxicological Basis	Recommended Action
Acute	above 0.04 µg/cm <sup>2</sup>	<u>All Routes:</u> Acute Oral (ATSDR, 1997) = 0.003 m/kg/d - ChE Inhibition (WOE, human/animal data)  DAF = 10%  LOC = 10X (1X inter-sp. human study)	relocate everyone within 48 hours

<sup>8</sup> Per sampling data materials provided to EPA/OPP via 7/24/2013 email correspondence with Tom Condon (EPA Region 1). An updated data summary from more recent sampling results was provided with Vermont’s comments to EPA/OPP (8/7/2013). As of the date of document completion the most recent sampling results have not been submitted nor evaluated by EPA/OPP and, therefore, only the previously evaluated data have been presented.

<sup>9</sup> The documentation of the calculations used by VDOH was sent to OPP in a PDF file for review. Any noted differences are based on a comparison of this document (and associated follow up phone conversations) with OPP’s methods based on the SOPs for Residential Exposure Assessment and toxicological data for chlorpyrifos.

Table 1. Vermont Action Levels and Associated Endpoints			
Exposure Duration	Action Range	Toxicological Basis	Recommended Action
Acute	above 0.004 $\mu\text{g}/\text{cm}^2$	<u>All Routes:</u> Acute Oral (ATSDR, 1997) = 0.003 m/k/d - ChE Inhibition (WOE, human/animal data)  DAF = 10%  LOC = 100X	relocate everyone within 1 week
Acute (sensitive populations)	above 0.0004 $\mu\text{g}/\text{cm}^2$	<u>All Routes:</u> Chronic Oral (EPA/OPP): BMDL <sub>10</sub> = 0.03 m/k/d - 10% ChE inhibition in rat dams (DNT)  DAF = 10%  LOC = 1,000X	relocate women of childbearing age and children < 12 years old within 1 week
Chronic (sensitive population)	below 0.0004 $\mu\text{g}/\text{cm}^2$	<u>All Routes:</u> Chronic Oral (EPA/OPP): BMDL <sub>10</sub> = 0.03 m/kg/d - 10% ChE inhibition in rat dams (DNT)  DAF = 10%  LOC = 1,000X	no action

### EPA/OPP Analysis

- EPA/OPP evaluated the analysis and data provided by VDOH. EPA/OPP used the *SOPs for Residential Exposure Assessment* to calculate values analogous to the Vermont computed action levels (i.e., they represent the total mass of deposited residue). The values, presented in Table 2 below, were calculated based on varying levels of concern (i.e., a level of concern (LOC) is defined by an appropriate margin of exposure, or MOE; in this case an appropriate MOE of 1, 10, 100, and 1,000 were considered).

<b>Table 2. EPA/OPP's Action Levels for Various LOCs and Populations</b>				
<b>Short-Term Action Level Residue (ug/cm<sup>2</sup>)</b>				
Population	LOC = 1	LOC = 10	LOC = 100*	LOC = 1,000
Adults	200	20	2.0	0.19
Children 1 to < 2	24	2.4	0.24	0.016
<b>Chronic Action Level Residue (ug/cm<sup>2</sup>)</b>				
Population	LOC = 1	LOC = 10	LOC = 100*	LOC = 1,000
Adults	43	4.3	0.43	0.025
Children 1 to < 2	6	0.6	0.060	NA

**Notes:**

\* EPA/OPP determined that an LOC = 100 was appropriate for use in the most current regulatory risk assessment of chlorpyrifos (2011 HHRA).

The calculation for each of these action levels is included as an attachment to this document. No action level residue could be determined for chronic exposures to children 1 to < 2 years old for an LOC = 1,000 due to the impact from dietary exposure.

- EPA/OPP calculated the above action levels using the Residential SOP calculators which are publicly available.<sup>10</sup> To define these action level estimates for different populations of interest (e.g., adults and small children who have high dermal exposure, and children exhibiting mouthing behaviors), EPA/OPP used a back-calculation approach beginning with the appropriate LOC and POD for each population and duration of interest. Then deposition values were input until the resulting MOEs were  $\geq$  the LOC for the particular scenario.

The toxicological inputs EPA/OPP used in its most recent regulatory risk assessment for chlorpyrifos are presented in Table 3 below<sup>11</sup>:

<b>Table 3. EPA/OPP's Action Levels and Associated Toxicological Doses and Endpoints and Points of Departure</b>		
<b>Exposure Duration</b>	<b>Action Range</b>	<b>Toxicological Basis</b>
Short- Term (1 to 30 days)	above 0.24 $\mu\text{g}/\text{cm}^2$	Oral: ST Incidental Oral: BMDL <sub>10</sub> = 0.1 m/k/d - CCA study

<sup>10</sup> <http://www.epa.gov/pesticides/science/residential-exposure-sop.html>

<sup>11</sup> The toxicological inputs used are consistent with those selected in the June 2011 *Chlorpyrifos Preliminary Human Health Risk Assessment for Registration Review*.

<b>Table 3. EPA/OPP's Action Levels and Associated Toxicological Doses and Endpoints and Points of Departure</b>		
<b>Exposure Duration</b>	<b>Action Range</b>	<b>Toxicological Basis</b>
		<u>Dermal:</u> S/IT Dermal: NOAEL = 5 m/k/d - 21 day dermal, ChE Inhibition  LOC = 100X
Chronic (> 6 months)	above 0.060µg/cm <sup>2</sup>	<u>All Routes:</u> Chronic Oral (EPA/OPP): BMDL <sub>10</sub> 0.03 m/kg/d - 10% ChE inhibition in rat dams (DNT)  DAF = 3%  LOC = 100X

Risk calculations were conducted and summarized in the tables below. Results based on EPA/OPP risk assessment inputs (i.e., SOPs and toxicological endpoints/PODs) and the VDOH action levels are presented in Table 4 below. The results indicate that, based on the VDOH action levels, EPA/OPP does not have a concern because MOEs in all scenarios are > 100. When actual sampling data are used (Table 5) EPA/OPP would only have a concern if risks are based on the maximum measured value in the “sentinel house” (the first house sampled by Vermont) where MOEs range from 6 to 91, and vary depending upon who is exposed and their exposure condition (i.e., carpet or hard floor). In all other cases including the mean residue level for the sentinel house, risks are not of concern based on the available sampling data using EPA/OPP inputs.

<b>Table 4. Risks (MOEs) Estimated Using EPA/OPP Methods and Pertinent PODs Coupled with Vermont Recommended Action Levels</b>				
<b>Exp. Scenario</b>	<b>Lifestage</b>	<b>VT Exposure Durations</b>	<b>VT Action Level Dep. Residues (µg/cm<sup>2</sup>)</b>	<b>Aggregated MOE*</b>
Carpet	Adults	Acute [EPA/OPP Short term PODs used]	0.04	4,600
	1 to < 2 years			820
Hard Surfaces	Adults			3,500
	1 to < 2 years			510
Carpet	Adults	Acute (sensitive populations) [EPA/OPP Short term PODs used]	0.004	8,300
	1 to < 2 years			2,300
Hard Surfaces	Adults			7,800
	1 to < 2 years			2,000

<b>Table 4. Risks (MOEs) Estimated Using EPA/OPP Methods and Pertinent PODs Coupled with Vermont Recommended Action Levels</b>				
<b>Exp. Scenario</b>	<b>Lifestage</b>	<b>VT Exposure Durations</b>	<b>VT Action Level Dep. Residues (<math>\mu\text{g}/\text{cm}^2</math>)</b>	<b>Aggregated MOE*</b>
	years			
Carpet	Adults	Chronic (sensitive population)	0.0004	2,700
	1 to < 2 years			860
Hard Surfaces	Adults			2,600
	1 to < 2 years			840

\* Aggregated MOE =  $1 / ((1/\text{Dermal MOE}) + (1/\text{Incidental Oral MOE}) + (1/\text{Dietary MOE}))$

<b>Table 5. Risks (MOEs) Estimated Using EPA/OPP Methods and Vermont Sampling Data</b>				
<b>Exp. Scenario</b>	<b>Lifestage</b>	<b>Exposure Durations</b>	<b>VT Action Level Dep. Residues (<math>\mu\text{g}/\text{cm}^2</math>)</b>	<b>Aggregated MOE*</b>
Carpet	Adults	Short-Term [Sentinel House – Sampled 8 Days Following Application]	4.0 (Maximum)	91
	1 to < 2 years			11
Hard Surfaces	Adults			57
	1 to < 2 years			6
Carpet	Adults		0.094 (Mean)	2,700
	1 to < 2 years			410
Hard Surfaces	Adults			1,900
	1 to < 2 years			240
Carpet	Adults	Chronic [All Other Data – Sampled 45 to 135 Days Following Application]	0.013 (Maximum)	1,800
	1 to < 2 years			470
Hard Surfaces	Adults			1,500
	1 to < 2 years			330
Carpet	Adults		0.00040 (Mean)	2,700
	1 to < 2 years			860
Hard Surfaces	Adults			2,700
	1 to < 2 years			840

\* Aggregated MOE =  $1 / ((1/\text{Dermal MOE}) + (1/\text{Incidental Oral MOE}) + (1/\text{Dietary MOE}))$

## **Issues For Consideration**

EPA/OPP evaluated VDOH's analysis and identified a number of issues for consideration. These include:

- EPA/OPP uses route- and duration-specific PODs and endpoints as appropriate. VDOH used acute and chronic oral (only) PODs for all analyses with a value for dermal absorption. The use of route specific dose administration data is typically considered more appropriate in risk assessment.
- In use of the oral POD to assess dermal exposures, Vermont adjusted the oral dose by a dermal exposure factor of 10% [an approach consistent with the Risk Assessment Guidance for Superfund (RAGS) Part E]. EPA/OPP uses a recommends a chlorpyrifos specific data-derived dermal absorption factor of 3% based on based on the ratio of the oral LOAEL of 0.3 mg/kg/day from the rat developmental neurotoxicity study to the dermal LOAEL of 10 mg/kg/day from the 21-day rat dermal study. This absorption factor is comparable to the dermal absorption (minimum 1-3%) estimated from human data in Nolan *et al.* (1982, MRID 00249203).
- VDOH did not use all inputs consistent with those recommended by the ***SOPs for Residential Exposure Assessment***. In particular, VDOH altered the exposure time (ET) inputs for time spent on hard surfaces and carpets to 8 hours for both the calculation of dermal and incidental oral exposures. Per Vermont's comments to EPA/OPP (8/7/2013), VDOH cited the use of data from the Exposure Factors Handbook 2011 edition. Specifically, VDOH used the total time spent indoors minus the time spent sleeping and napping to estimate the time spent indoors as 8 hours, instead of the 4 hours used for children in EPA/OPP's Residential SOPs.<sup>12</sup> The exposure times recommended in the 2012 Residential SOPs are based on the Exposure Factors Handbook 2011 Edition which provides information on total time spent in a residence and time spent in various rooms within a residence and were selected with the intention of resulting in health protective risk outcomes. In making this adjustment to EPA/OPP's Residential SOPs, VDOH did not appropriately account for the factors considered in the development of the SOPs which address the total exposure of those being considered in risk assessment. These factors are discussed extensively in the SOPs themselves and were also a topic for consideration at the FIFRA Scientific Advisory Panel review of the SOPs.<sup>13</sup>
- Acute exposures were assessed by VDOH. EPA/OPP did not consider assessment of acute exposures given that all residences were treated with chlorpyrifos days and months prior to sampling and also because EPA/OPP assessments typically account for this exposure pattern. Further, based on the methods and toxicological endpoints/PODs used by EPA/OPP, the short-term assessment results in action levels protective for acute exposures (i.e., action levels are lower).

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<sup>12</sup> Per the 2012 Residential SOPs for Residential Exposure Assessment, the same approach as used by Vermont (the time spent indoors minus the time spent sleeping and napping) was applied to define time spent on carpeted surfaces. The 2012 SOPs recommend an exposure time on carpeted surfaces of 8 hours for adults; however, an exposure time of only 4 hours is recommended for children. The exposure times recommended in the 2012 SOPs for adults and children on hard surfaces, 2 hours, was derived from total time spent daily in kitchens and bathrooms.

<sup>13</sup> <http://www.epa.gov/scipoly/sap/meetings/2009/100609meeting.html>

- Existing data for chlorpyrifos indoors suggest no aerosolized particulate exists in the residences following the day of application. Therefore, inhalation risks are not likely of concern for the inhabitants of the affected residences. Neither the action levels calculated by VDOH, nor the EPA/OPP calculations consider inhalation exposure.
- VDOH estimated action levels on LOCs ranging from 10 to 1,000 depending upon which scenario is considered. EPA/OPP has determined that an LOC of 100 is adequate for the assessment of all risk outcomes considering route and duration specific PODs have been used; however, a number of uncertainties have been identified that may result in the potential to underestimate actual exposure levels in chlorpyrifos-treated homes. These uncertainties are discussed below. For purpose of risk characterization, EPA/OPP presented a range of action values as calculated for various LOCs and populations in Table 2 of this document.

### Discussion of Uncertainties

EPA/OPP conducted an assessment of residential exposures to chlorpyrifos in support of a request from the state of Vermont for assistance in assessing exposure/risk from use of the pesticide indoors as an apparent misuse. The EPA/OPP assessment employs the approach typically used for the regulation of residential pesticide products, including: application of the methods and assumptions outlined in the 2012 *SOPs for Residential Exposure Assessment* to evaluate indoor pesticide exposure; and application of the best data available to assess indoor exposures, including wipe sample data submitted by the state collected from homes suspected to have been treated with chlorpyrifos. While this approach is considered health protective for the purpose of evaluating potential risks associated with the application following the label directions of a registered pesticide, the assessment of pesticide misuse is unique. Therefore, the risk estimates developed by EPA/OPP may underestimate the risks due to exposure from such misuse.

Examples of how the state of Vermont's exposure estimates may underestimate actual exposures levels include:

1) Chlorpyrifos residue data (wipe sample) collection: Vermont sampled for the presence of chlorpyrifos surface residues in homes suspected to have been treated. EPA/OPP believes the wipe sample method used (prewashed cotton ball swabs soaked with methanol) is adequate for efficient collection of chlorpyrifos residues present on the surface; however, according to Vermont, this methodology limited them to sampling hard surfaces only. Examples of wipe sample locations reported by Vermont include: baseboards, boxes, furniture tops, mirrors, walls, and windows. It is likely that adults or children in the treated homes could have contact with these surfaces, as well as with carpeted floors, mattresses, and sofas. It is our understanding that in the sentinel residence, a mattress was treated to the extent that it took 2 weeks for it to dry out. Therefore, it is possible that indoor residue levels may have exceeded those predicted by wiping hard surfaces alone.

Further, analysis of chlorpyrifos surface residues in a home sampled 8 days following the initial application - and with the highest measured residues of all houses sampled- suggests the potential for variability. Results from the home show that residues from 1 of the 8 hard surface

samples collected is greater than (2.4X) the next highest sample, and well above (4.2X) the mean of all samples from the home. Therefore, dependent on sampling location within a treated home, the highest residues may not have been captured. Because of this variability in wipe results, and the fact that carpeted floors, mattresses, and sofas, which may have higher residues than hard surfaces, were not sampled, there is the potential to underestimate the actual chlorpyrifos concentrations in these homes.

2) Chlorpyrifos oxon: Chlorpyrifos is activated by oxidative desulfuration, reacting to form the more toxic and potent acetyl cholinesterase (AChE) inhibitor, chlorpyrifos oxon. Therefore, there is potential for inhabitants of the chlorpyrifos-treated homes in Vermont to be exposed to the parent compound, chlorpyrifos, as well as chlorpyrifos oxon as the chlorpyrifos is transformed. The residue wipe sample collection efforts undertaken by the state to date have measured only for the parent compound (chlorpyrifos only). Data to determine the presence and/or levels of chlorpyrifos oxon residue is an uncertainty of the assessment of exposures/risk from the misuse of chlorpyrifos in Vermont. Further, the source of chlorpyrifos applied indoors appears to be from existing stocks of residential products cancelled in 2001. It is possible that parent chlorpyrifos may have degraded over more than a decade in storage, thus increasing the amount of chlorpyrifos oxon present relative to parent.

In EPA/OPP's July 2011 chlorpyrifos human health risk assessment (HHRA), *Preliminary Human Health Risk Assessment for Registration Review*, toxicity factors were developed to estimate the potency of chlorpyrifos oxon relative to chlorpyrifos for the aggregate assessment. A chronic toxicity factor of 18.0 was derived from the bench mark dose (BMD) analysis of inhibition of RBC ChE in adult female rats (adult male rats not examined since females rats were determined to be more sensitive in the acute study) observed in the repeated phase of the comparative cholinesterase assay (CCA study). A chronic toxicity factor of 18 was recommended for chlorpyrifos oxon (compared to chlorpyrifos). An acute toxicity factor was also recommended in the 2011 HHRA; however, because the basis of the chronic toxicity factor is an 11 day repeat dosing CCA study, it is considered appropriate for use to characterize exposures/risks estimated for short-term (1 to 30 days), as well as chronic exposure durations.

Based on the uncertainties of the chlorpyrifos (and potential chlorpyrifos oxon) surface residue concentrations in the residences treated indoors as an apparent misuse, the state of Vermont may wish to consider evaluating risk estimates across a range of potential chlorpyrifos residue concentrations. For example, the state could consider the risks taking into account the presence of the more potent oxon following treatment indoors, and/or the lack of residue data from surfaces such as carpeted floors, mattresses, and sofas, and/or potentially higher residue concentration levels than those measured in wipe samples.

## Attachment – EPA/OPP Detailed Calculations

The following tables present the dermal and oral, and combined exposure/risk calculations used to estimate (back-calculated) chlorpyrifos deposited, or action level residues. Tables 6, 7, and 8 present short-term dermal, incidental oral, and combined dermal/oral exposures/risks and estimated action level residues respectively. Tables 9, 10, and 11 present chronic dermal, incidental oral, and combined dermal/oral exposures/risks, respectively. The exposure scenario, children 1 to < 2 years old contacting hard surfaces, resulting in the lowest, or most health protective, estimated action level residues are bolded.

Table 6. Short-Term: Action Level Residues Estimated for Dermal Exposures to Chlorpyrifos from Indoor Misuse											
Exposure Scenario		Lifestage	Action Level Residue (ug/cm <sup>2</sup> ) <sup>a</sup>	Fraction transferred <sup>b</sup>	Transferable Residue (ug/cm <sup>2</sup> ) <sup>c</sup>	TC (cm <sup>2</sup> /hr) <sup>d</sup>	ET (hr/day) <sup>e</sup>	Conversion factor (mg/ug)	Exposure (mg/day) <sup>f</sup>	Absorbed Dose (mg/kg/day) <sup>g</sup>	ST Dermal MOE <sup>h</sup>
Broadcast	Carpet	Adults	3.5	0.02	0.07	6,800	8	1.0E-03	3.81	0.048	110
		1 to <2 years	0.42	0.02	0.0084	1,800	4	1.0E-03	0.06	0.0055	910
	Hard surface	Adults	2.0	0.13	0.26	6,800	2	1.0E-03	3.54	0.044	110
		<b>1 to &lt;2 years</b>	<b>0.24</b>	<b>0.13</b>	<b>0.03081</b>	<b>1,800</b>	<b>2</b>	<b>1.0E-03</b>	<b>0.11</b>	<b>0.01</b>	<b>500</b>

- Action Level Residue (ug/cm<sup>2</sup>) is the back-calculated total deposited residue value that results in a combined (all routes of exposure) MOE of  $\geq 100$  (LOC = 100).
- Fraction transferred is based on chlorpyrifos-specific data provided in HED's 2012 Residential SOPs/Indoor Environments.
- Transferable residue (ug/cm<sup>2</sup>) = Action level residue (ug/cm<sup>2</sup>) \* fraction transferred (0.02 for carpets and 0.13 for hard surfaces, chlorpyrifos-specific inputs).
- TC = Transfer coefficient (cm<sup>2</sup>/hr).
- ET = exposure time (hr/day).
- Exposure (mg/day) = Action Level Residue (ug/cm<sup>2</sup>) \* Fraction transferred \* Transfer coefficient (cm<sup>2</sup>/hr) \* Exposure time (hr/day) \* Conversion factor (0.001 mg/ug).
- Absorbed Dose (mg/kg/day) = Exposure (mg/day) / Body Weight (80 kg for adults and 11 kg for children 1 to < 2 years old).
- Dermal MOE = PoD (mg/kg/day) / Absorbed Dose (mg/kg/day), where short-term dermal POD = 5 mg/kg/day from a 21-day dermal study; LOC = 100.

**Table 7. Short-term: Incidental Oral Risks Calculated for Exposures to Chlorpyrifos from Indoor Misuse**

Exp. Scenario	Life-stage	F <sub>aihands</sub>	DE	SA <sub>H</sub>	HR	F <sub>m</sub>	ET	Replenishment interval (min)	N_Replen	SE	Freq_HtM	Abs. Dose (m/k/d)	ST Incidental Oral MOE
		Fraction ai on hands compared to total surface residue	Derm. Exp. (mg)	Surface area of 1 hand (cm <sup>2</sup> )	Hand residue loading (mg/cm <sup>2</sup> )	Frac. hand mouthed	Exp. Time (hrs/day)		# replenishment intervals per hour (intervals/hr)	Fraction Saliva Extraction	Number of hand-to-mouth contacts events per hour (events/hr)		
Broadcast													
Carpet	1 to <2 years	0.15	0.060	150	3.0x10 <sup>-5</sup>	0.13	4	15	4	0.48	20	8.3x10 <sup>-4</sup>	120
Hard Surfaces	1 to <2 years	0.15	0.11	150	5.6x10 <sup>-5</sup>	0.13	2	15	4	0.48	20	7.6x10 <sup>-4</sup>	130

- F<sub>aihands</sub> = Fraction ai on hands compared to total surface residue based on data presented in the 2012 Residential SOPs/Indoor Environment.
- DE = Dermal Exposure value.
- SA<sub>H</sub> = Surface area of one hand (cm<sup>2</sup>).
- HR = Hand Residue Loading (mg/cm<sup>2</sup>) = (F<sub>aihands</sub> \* Dermal exposure) / (SA<sub>H</sub> \* 2).
- F<sub>M</sub> = Fraction of hand mouthed.
- ET = Exposure Time (hr/day).
- N\_Replen = Number of Replenishment Intervals per hour (intervals/hr) assuming a 15 minute replenishment interval.
- SE = Saliva Extraction Factor.
- Freq\_HtM = Number of hand-to-mouth contacts events per hour (events/hr).
- Absorbed Dose (mg/kg/day) = {(HR \* F<sub>M</sub> \* SA<sub>H</sub>) \* (ET \* N\_Replen) \* [1-(1-SE)<sup>(Freq\_Replen / N\_Replen)</sup>]} / Body Weight (11 kg).
- Incidental Oral MOE = POD (mg/kg/day) / Absorbed Dose (mg/kg/day); short-term incidental oral POD 0.1 mg/kg/day; LOC = 100.

Table 8. Short-Term Aggregate Risk Calculations						
Population	Hard Surfaces Exposure Scenario					
	LOC for Aggregate Risk <sup>1</sup>	Dietary MOE <sup>2</sup>	MOE Oral Residential Exposure <sup>3</sup>	MOE Dermal Residential Exposure <sup>4</sup>	Short-Term Aggregate MOE (food, water, and residential) <sup>5</sup>	Action Level Residue (ug/cm <sup>2</sup> ) <sup>6</sup>
Adults	100	9,000	NA	110	100	2.0
Children 1 to < 2 years old		2,900	130	500		<b>0.24</b>

<sup>1</sup> LOC [10X for interspecies extrapolation, 10X for intraspecies variation and a 1X FQPA safety factor].

<sup>2</sup> MOE dietary = [(short-term oral NOAEL)/(chronic dietary exposure)].

<sup>3</sup> MOE oral = [(short-term oral NOAEL)/(hand-to-mouth residential exposure)].

<sup>4</sup> MOE dermal = [(short-term dermal NOAEL)/(high end dermal residential exposure)]

<sup>5</sup> MOE Aggregate = 1/[(1/MOE dietary) + (1/MOE oral) + (1/MOE dermal) + (1/MOE inhalation)]

<sup>6</sup> Action Level Residue (ug/cm<sup>2</sup>) is the back-calculated total deposited residue value that results in a combined (all routes of exposure) MOE of  $\geq 100$  (LOC = 100).

**Table 9. Chronic: Action Level Residues Calculated for Dermal Exposures to Chlorpyrifos from Indoor Misuse**

Exposure Scenario		Lifestage	Action Level Residue (ug/cm <sup>2</sup> ) <sup>a</sup>	Fraction transferred <sup>b</sup>	Transferable Residue (ug/cm <sup>2</sup> ) <sup>c</sup>	TC (cm <sup>2</sup> /hr) <sup>d</sup>	ET (hr/day) <sup>3</sup>	Conversion factor (mg/ug)	Exposure (mg/day) <sup>f</sup>	Absorbed Dose (mg/kg/day) <sup>g</sup>	Chronic Dermal MOE <sup>h</sup>
Broadcast	Carpet	Adults	0.70	0.02	0.014	6,800	8	1.0E-03	0.762	0.00029	110
		1 to <2 years	0.11	0.02	0.0022	1,800	4	1.0E-03	0.016	0.000043	690
	Hard surface	Adults	0.43	0.13	0.0559	6,800	2	1.0E-03	0.760	0.00029	110
		<b>1 to &lt;2 years</b>	<b>0.060</b>	<b>0.13</b>	<b>0.0078</b>	<b>1,800</b>	<b>2</b>	<b>1.0E-03</b>	<b>0.028</b>	<b>0.000077</b>	<b>390</b>

- i. Action Level Residue (ug/cm<sup>2</sup>) is the back-calculated total deposited residue value that results in a combined (all routes of exposure) MOE of  $\geq 100$  (LOC = 100).
- j. Fraction transferred is based on chlorpyrifos-specific data provided in HED's 2012 Residential SOPs/Indoor Environments.
- k. Transferable residue (ug/cm<sup>2</sup>) = Action level residue (ug/cm<sup>2</sup>) \* fraction transferred (0.02 for carpets and 0.13 for hard surfaces, chlorpyrifos-specific inputs).
- l. TC = Transfer coefficient (cm<sup>2</sup>/hr).
- m. ET = exposure time (hr/day).
- n. Exposure (mg/day) = Action Level Residue (ug/cm<sup>2</sup>) \* Fraction transferred \* Transfer coefficient (cm<sup>2</sup>/hr) \* Exposure time (hr/day) \* Conversion factor (0.001 mg/ug).
- o. Absorbed Dose (mg/kg/day) = Exposure (mg/day) \* Absorption Factor (0.03)/ Body Weight (80 kg for adults and 11 kg for children 1 to < 2 years old).
- p. Dermal MOE = PoD (mg/kg/day) / Absorbed Dose (mg/kg/day), where chronic dermal POD = 0.03 mg/kg/day from an oral study; LOC = 100.

**Table 10. Chronic: Incidental Oral Risks Calculated for Exposures to Chlorpyrifos from Indoor Misuse – Linked to Dermal Exposures**

Exposure Scenario	Life-stage	F <sub>aihands</sub>	DE	SA <sub>H</sub>	HR	F <sub>m</sub>	ET	Replenishment interval (min)	N_Replen	SE	Freq_HtM	Abs. Dose (m/k/d)	Chronic Incidental Oral MOE
		Fraction ai on hands compared to total surface residue	Derm. Exp. (mg)	Surface area of 1 hand (cm <sup>2</sup> )	Hand residue loading (mg/cm <sup>2</sup> )	Frac. hand mouthed	Exp. Time (hrs/day)		# replenishment intervals per hour (intervals/hr)	Fraction Saliva Extraction	Number of hand-to-mouth contacts events per hour (events/hr)		
Broadcast													
Carpet	1 to <2 years	0.15	0.016	150	7.9x10 <sup>-6</sup>	0.13	4	15	4	0.48	20	2.2x10 <sup>-4</sup>	140
Hard Surfaces	1 to <2 years	0.15	0.028	150	1.4x10 <sup>-5</sup>	0.13	2	15	4	0.48	20	1.9x10 <sup>-4</sup>	160

- l. F<sub>aihands</sub> = Fraction ai on hands compared to total surface residue based on data presented in the 2012 Residential SOPs/Indoor Environment.
- m. DE = Dermal Exposure value.
- n. SA<sub>H</sub> = Surface area of one hand (cm<sup>2</sup>).
- o. HR = Hand Residue Loading (mg/cm<sup>2</sup>) = (F<sub>aihands</sub> \* Dermal exposure) / (SA<sub>H</sub> \* 2).
- p. F<sub>M</sub> = Fraction of hand mouthed.
- q. ET = Exposure Time (hr/day).
- r. N\_Replen = Number of Replenishment Intervals per hour (intervals/hr) assuming a 15 minute replenishment interval.
- s. SE = Saliva Extraction Factor.
- t. Freq\_HtM = Number of hand-to-mouth contacts events per hour (events/hr).
- u. Absorbed Dose (mg/kg/day) = {(HR \* F<sub>M</sub> \* SA<sub>H</sub>) \* (ET \* N\_Replen) \* [1-(1-SE)<sup>(Freq\_Replen / N\_Replen)</sup>]} / Body Weight (11 kg).
- v. Incidental Oral MOE = POD (mg/kg/day) / Absorbed Dose (mg/kg/day); chronic incidental oral POD 0.03 mg/kg/day; LOC = 100.

Table 11. Chronic Aggregate Risk Calculations						
Population	Hard Surfaces Exposure Scenario					
	LOC for Aggregate Risk <sup>1</sup>	Dietary MOE <sup>2</sup>	MOE Oral Residential Exposure <sup>3</sup>	MOE Dermal Residential Exposure <sup>4</sup>	Chronic Aggregate MOE (food, water, and residential) <sup>5</sup>	Action Level Residue (ug/cm <sup>2</sup> ) <sup>6</sup>
Adults	100	2,700	NA	110	100	0.43
Children 1 to < 2 years old		880	160	390		<b>0.060</b>

<sup>1</sup> LOC [10X for interspecies extrapolation, 10X for intraspecies variation and a 1X FQPA safety factor].

<sup>2</sup> MOE dietary = [(chronic oral NOAEL)/(chronic dietary exposure)].

<sup>3</sup> MOE oral = [(chronic oral NOAEL)/(hand-to-mouth residential exposure)].

<sup>4</sup> MOE dermal = [(short- or intermediate-term dermal NOAEL)/(high end dermal residential exposure

<sup>5</sup> MOE Aggregate = 1/[(1/MOE dietary) + (1/MOE oral) + (1/MOE dermal) + (1/MOE inhalation)]

<sup>6</sup> Action Level Residue (ug/cm<sup>2</sup>) is the back-calculated total deposited residue value that results in a combined (all routes of exposure) MOE of  $\geq 100$  (LOC = 100).

## **Attachment – Exposure Algorithms**

Algorithms Used To Calculate Exposures from Dermal and Oral Exposures Excerpted From  
SOPs Used To Regulate Residential Pesticide Products

### **Post-Application Dermal Exposure Algorithm (hard surfaces and carpets)**

The algorithm to calculate exposure is as follows:

where:

E = exposure (mg/day);  
TR = indoor surface transferable residue ( $\mu\text{g}/\text{cm}^2$ );  
TC = transfer coefficient ( $\text{cm}^2/\text{hr}$ );  
ET = exposure time (hr/day); and  
CF1 = conversion factor (0.001 mg/ $\mu\text{g}$ ).

If chemical-specific TR data are available, this is preferred and should be used to calculate exposure. However, if chemical-specific TR data are not available, then TR can be calculated using the following formula:

where:

TR = indoor surface transferable residue ( $\mu\text{g}/\text{cm}^2$ );  
DepR = deposited residue ( $\mu\text{g}/\text{cm}^2$ ), based on (in order of preference):  
(1) Chemical-specific residue deposition data ( $\mu\text{g}/\text{cm}^2$ ),  
(2) Application rate (lb ai/area), or  
(3) Default residue based on type of application ( $\mu\text{g}/\text{cm}^2$ ); and  
F<sub>ai</sub> = fraction of ai available for transfer from carpet or hard surface (unitless).

Absorbed dermal dose, normalized to body weight, are calculated as:

where:

D = dose (mg/kg-day);  
E = exposure (mg/day);  
AF = absorption factor; and  
BW = body weight (kg).

Table 12. Indoor Environments (Hard Surfaces and Carpets) – Inputs for Residential Post-application Dermal Exposure				
Algorithm Notation	Exposure Factor (units)		Point Estimate(s)	
TR	Transferable residue (µg/cm²)		Estimated using the deposited residue, or “action level” residue and the fraction transferred following application (F <sub>ai</sub> )	
DepR	Deposited residue (µg/cm²)		For the purpose of this document, the deposited residue, or “action level” residue, was determined by back calculating to a level resulting in risks (MOEs) that are ≥ HED’s level of concern (i.e., an MOE ≥ 100).	
F <sub>ai</sub>	Fraction of DepR as TR following application:	*Chlorpyrifos specific		
		Carpets		0.02
		Hard surfaces		0.13
TC	Transfer Coefficient (cm²/hr)	Adult		6,800
		Children 1 < 2 years old		1,800
ET	Exposure Time (hrs/day)	Adults	Carpets	8
			Hard Surfaces	2
		Children 1 < 2 years old	Carpets	4
			Hard Surfaces	2
BW	Body weight (kg)	Adult		80
		Children 1 < 2 years old		11

### **Post-application Hand-to-Mouth Exposure Algorithm**

Exposure from hand-to-mouth activity is calculated as follows (based on algorithm utilized in SHEDS-Multimedia):

where:

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E	= exposure (mg/day);
HR	= hand residue loading (mg/cm <sup>2</sup> );
F <sub>M</sub>	= fraction hand surface area mouthed / event (fraction/event);
ET	= exposure time (hr/day);
SA <sub>H</sub>	= surface area of one hand (cm <sup>2</sup> );
N_Replen	= number of replenishment intervals per hour (intervals/hour);
SE	= saliva extraction factor (i.e., mouthing removal efficiency); and
Freq_HtM	= number of hand-to-mouth contacts events per hour (events/hour).

and

where:

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HR	= hand residue loading (mg/cm <sup>2</sup> );
Fai <sub>hands</sub>	= fraction ai on hands compared to total surface residue from jazzercise study (unitless);
DE	= dermal exposure (mg); and
SA <sub>H</sub>	= typical surface area of one hand (cm <sup>2</sup> ).

and

Dose, normalized to body weight, is calculated as:

where:

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D	= dose (mg/kg-day);
E	= exposure (mg/day); and
BW	= body weight (kg).

Table 13. Indoor Environments – Inputs for Residential Post-application Hand-to-Mouth Exposure				
Algorithm Notation	Exposure Factor (units)			Point Estimate(s)
F <sub>ai_hands</sub>	Fraction of ai on hands from jazzercise study (unitless)			0.15
DE	Dermal exposure calculated (see using dermal algorithm above) (mg)			Calculated
HR	Residue available on the hands (mg/cm <sup>2</sup> )			Calculated
SA <sub>H</sub>	Surface area of one hand (cm <sup>2</sup> )	Children 1 < 2 years old		150
F <sub>M</sub>	Fraction of hand mouthed per event (fraction/event)			0.13
N_Replen	Replenishment intervals per hour (intervals/hr)			4
ET	Exposure time (hours per day)	Children 1 < 2 years old	Carpets	4
			Hard Surfaces	2
SE	Saliva extraction factor (fraction)			0.48
Freq_HtM	Hand-to-mouth events per hour (events/hr)	Children 1 < 2 years old		20
BW	Body Weight (kg)	Children 1 < 2 years old		11

## **Attachment - Chlorpyrifos Toxicity**

Chlorpyrifos, like other organophosphates, inhibits the enzyme acetylcholinesterase which leads to accumulation of acetylcholine and ultimately to neurotoxicity. In previous chlorpyrifos risk assessments, including the June 2011 *Chlorpyrifos Preliminary Human Health Risk Assessment for Registration Review* (HHRA)<sup>14</sup>, the Agency concluded that data on the inhibition of cholinesterase (ChE) provided the most sensitive dose-response data for use in deriving points of departure (POD) for all durations, routes of exposure, and lifestages. This assessment relies on the endpoint selection from the 2011 HHRA.

The toxicity database of laboratory animal studies spans multiple routes of exposure (oral, dermal, and inhalation), animal species, lifestages, and durations. The database consists of studies that address different durations of exposure from a single exposure day (acute) to subchronic and chronic toxicity. The metabolism and pharmacokinetics of chlorpyrifos are well-characterized due to a variety of studies in different species and lifestages. The studies used to complete this assessment are of high quality and provide information that are appropriate for evaluating risks associated with single day exposures which are the focus of this assessment. Chlorpyrifos is not likely to be carcinogenic to humans, based on the lack of evidence of carcinogenicity in studies in rats and mice and the absence of a mutagenicity concern. There was no sign of immunotoxicity in the guideline study at the highest dose tested.

### **Dose-Response Assessment**

The endpoints and PODs used for this analysis are summarized below. A 1x FQPA safety factor (SF) was used in all cases. Endpoints and PoDs for risk assessment represent the most sensitive compartment (i.e., RBC, lung or brain) from the most sensitive sex in both juvenile (> PND11) and adult rats for the following exposure scenarios.

#### ***Incidental Oral***

For the short-term incidental oral exposure scenario and for exposures through the diet, the results of the 11 day repeat phase of an oral CCA study (MRID 48139301) indicated inhibition of RBC ChE in male PND11 rats as the most sensitive endpoint. A BMDL<sub>10</sub> of 0.1 mg/kg/day was derived from a BMD analysis of the dose- response data.

Chronic oral risks were assessed using a chronic POD of 0.03 mg/kg/day (BMDL<sub>10</sub>) selected from pregnant (GD6-20) rats exposed to chlorpyrifos in the developmental neurotoxicity study (MRID 44556901, Hoberman *et al.* 1998a,b) on the basis of inhibition of RBC ChE in pregnant dams. This PoD was supported by a WOE evaluation of multiple studies including an oral gavage study in pregnant (GD6-LD10) rats (MRID 44648101) and the new CCA study. A total uncertainty factor of 100X is appropriate for assessment of incidental oral exposures [10X for interspecies extrapolation, 10X for intraspecies variation and a 1X FQPA safety factor].

#### ***Dermal***

A short-/intermediate-term dermal PoD was selected from a 21-day dermal toxicity study (MRID 40972801) in rats based on plasma and red blood cell ChE inhibition (NOAEL = 5 mg/kg/day).

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<sup>14</sup> [www.regulations.gov](http://www.regulations.gov) (docket ID EPA-HQ-OPP-2008-0850-0025)

The use of the 21-day dermal toxicity study is appropriate for durations up to 6 months as it is expected that steady state ChE inhibition would have been reached by approximately 21 days of dermal exposure. The Agency has previously shown (USEPA, 2001; preliminary organophosphate cumulative risk assessment) that at or near 3-4 weeks of exposure the degree of inhibition following repeated dosing with OPs does not change with increasing duration but instead remains approximately the same.

Chronic dermal exposures were assessed using the chronic POD of 0.03 mg/kg/day (BMDL<sub>10</sub>) described previously. A dermal absorption factor of 3% was used to adjust the dose from the developmental neurotoxicity study to a dermal equivalent. The dermal absorption factor of 3% was estimated based on the ratio of the oral LOAEL of 0.3 mg/kg/day from the rat developmental neurotoxicity study (MRIDs 44556901, 44661001) to the dermal LOAEL of 10 mg/kg/day from the 21-day rat dermal study (MRID 40972801) for plasma and red blood cell cholinesterase inhibition. This absorption factor is comparable to the dermal absorption (minimum 1-3%) estimated from human data in Nolan *et al.* (1982, MRID 00249203) by back-calculating chlorpyrifos exposure based on urinary levels of TCP.

<b>Table 14. Summary of Toxicological Doses and Endpoints and Points of Departure for Chlorpyrifos for Use in Assessment of Indoor Residential and Dietary Exposures/Risks</b>		
<b>Exposure Scenario</b>	<b>Point of Departure (mg/kg/day)</b>	<b>Study and Toxicological Effects</b>
Chronic Oral	BMDL <sub>10</sub> = 0.03  UF <sub>A</sub> = 10x UF <sub>H</sub> = 10x FQPA SF = 1x  LOC is an MOE = 100	Inhibition of RBC ChE in rat dams (GD 6 – 20). Weight of evidence from studies including: <ul style="list-style-type: none"> <li>• Developmental neurotoxicity study in pregnant (GD 6 - 20) rats (MRID 44556901)</li> <li>• Gavage study in pregnant (GD 6 – LD10) rats (MRID 44648101)</li> </ul>
Short-Term Oral (1 – 30 days)	BMDL <sub>10</sub> = 0.1  UF <sub>A</sub> = 10x UF <sub>H</sub> = 10x FQPA SF = 1x  LOC is an MOE = 100	Inhibition of RBC ChE in PND 11 male rats. <ul style="list-style-type: none"> <li>• 11 day repeat oral CCA study in the rat (MRID 48139301).</li> </ul>
Intermediate – term Oral (1-6 months)	BMDL <sub>10</sub> = 0.03  UF <sub>A</sub> = 10x UF <sub>H</sub> = 10x FQPA SF = 1x  LOC is an MOE = 100	See Chronic Dietary.
Dermal Short- (1 – 30 days) and Intermediate-	NOAEL = 5 mg/kg/day  UF <sub>A</sub> = 10x UF <sub>H</sub> = 10x	Plasma and RBC ChE inhibition.  21-day dermal study (NOAEL) and 4 day probe study (LOAEL) in adult rats (MRID 40972801).

**Table 14. Summary of Toxicological Doses and Endpoints and Points of Departure for Chlorpyrifos for Use in Assessment of Indoor Residential and Dietary Exposures/Risks**

Exposure Scenario	Point of Departure (mg/kg/day)	Study and Toxicological Effects
Term (1-6 months)	FQPA SF = 1x  LOC is an MOE=100  Dermal Absorption: 3%	